

CLAIMS

1. A compound comprising a target specific portion and an effector portion
wherein:
- 5
- (i) the target specific portion comprises or consists of a monoclonal antibody having specificity for oncofoetal fibronectin, or a fragment or variant thereof which retains the binding specificity for oncofoetal fibronectin of the parent monoclonal antibody; and
- 10
- (ii) the effector portion comprises or consists of interleukin-12, or a functional fragment or variant thereof
- characterised in the monoclonal antibody having specificity for oncofoetal fibronectin binds to a region of oncofoetal fibronectin other than the ED-B region.
- 15
2. A compound according to Claim 1 wherein the target specific portion is capable of binding to an amino acid sequence present in fibronectin expressed in both fetal and normal adult tissue.
- 20
3. A compound according to Claim 1 or 2 wherein the target specific portion is capable of binding an amino acid sequence within the repeat 7 domain of fibronectin.
- 25
4. A compound according to any one of Claims 1 to 3 wherein the target specific portion is specific for human oncofoetal fibronectin.
- 30
5. A compound according to any one of Claims 1 to 4 wherein the monoclonal antibody having specificity for oncofoetal fibronectin is a BC1 antibody, or an antibody capable of competing with the binding of a BC1 antibody to oncofoetal fibronectin.

6. A compound according to Claim 5 wherein the monoclonal antibody having specificity for oncofoetal fibronectin is a BC1 antibody.
- 5 7. A compound according to any one of the preceding claims wherein the monoclonal antibody is a human or humanised antibody.
8. A compound according to Claim 6 or 7 wherein the compound binds to oncofoetal fibronectin more tightly than the parent monoclonal antibody.
- 10 9. A compound according to Claim 8 wherein the compound binds to oncofoetal fibronectin more at least 2-fold tighter than the parent monoclonal antibody.
- 15 10. A compound according to Claim 8 or 9 wherein the compound binds to oncofoetal fibronectin at least 10-fold tighter than the parent BC1 antibody binds to oncofoetal fibronectin.
- 20 11. A compound according to any one of the preceding claims wherein the target specific portion comprises a polypeptide of SEQ ID NO: 1.
12. A compound according to any one of the preceding claims wherein the target specific portion comprises a polypeptide of SEQ ID NO: 2.
- 25 13. A compound according to Claim 11 or 12 wherein the target specific portion comprises a polypeptide of SEQ ID NO: 1 and a polypeptide SEQ ID NO: 2.
- 30 14. A compound according to any one of the preceding claims wherein the target specific portion comprises or consists of an antigen binding fragment of a monoclonal antibody having specificity for oncofoetal fibronectin.

15. A compound according to Claim 14 wherein the target specific portion comprises or consists of an antigen binding fragment selected from the group consisting of Fab-like molecules, such as Fab and F(ab')₂, Fv molecules, disulphide-linked Fv molecules, ScFv molecules and single domain antibodies (dAbs).
16. A compound according to any one of the preceding claims wherein the target specific portion comprises one or more antibody constant regions.
17. A compound according to Claim 16 wherein the one or more antibody constant regions comprises or consists of a CH1 domain.
18. A compound according to any one of the preceding claims further comprising an Fc moiety.
19. A compound according to Claim 18 wherein the Fc moiety is derived from human IgG1.
20. A compound according to any one of the preceding claims wherein the target specific portion comprises or consists of a whole BC1 antibody.
21. A compound according to any one of the preceding claims wherein the effector portion comprises or consists of human interleukin-12, or a functional fragment or variant thereof.
22. A compound according to any one of the preceding claims wherein the effector portion comprises or consists of a single-chain interleukin-12.
23. A compound according to any one of Claim 22 wherein the single chain IL-12 consists of an IL-12p35 domain and an IL-12p40 domain.

24. A compound according to any one of Claim 23 wherein the IL-12p35 domain is conjugated to the IL-12p40 domain by a disulphide bond.
25. A compound according to any one of the preceding claims wherein the compound is a fusion protein.
26. A compound according to any one of the preceding claims wherein the target specific portion is fused to the effector portion.
27. A compound according to Claim 26 comprising an immunoglobulin heavy chain fused to the effector portion.
28. A compound according to Claim 27 wherein the immunoglobulin heavy chain and the effector portion are joined via a mutated linker sequence.
29. A compound according to Claim 28 wherein the linker comprises or consists of the amino acid sequence ATATPGAA (SEQ ID NO. 5).
30. A compound according to any one of the preceding claims wherein the compound comprises a polypeptide of SEQ ID NO:6
31. A compound according to any one of the preceding claims wherein the compound comprises a polypeptide of SEQ ID NO:7.
32. A compound according to Claim 30 and 31 wherein the compound comprises a polypeptide of SEQ ID NO:6 and a polypeptide of SEQ ID NO:7.
33. A compound according to any one of Claims 30 to 32 further comprising a polypeptide of SEQ ID 4 linked by disulphide bond to the polypeptide of SEQ ID NO:6.

34. A fusion protein comprising antibody V regions directed against oncofoetal fibronectin, an Fc moiety, and an interleukin-12 moiety.
- 5 35. A nucleic acid molecule encoding a compound according to any one of Claims 1 to 34, or a target specific portion, effector portion or component polypeptide thereof.
- 10 36. A nucleic acid molecule according to Claim 35 wherein the molecule comprises one or more of the nucleotide sequences selected from the groups consisting of SEQ ID NOS: 8 to 10.
37. A nucleic acid molecule according to Claim 36 wherein the molecule comprises the nucleotide sequence of SEQ ID NO:8.
- 15 38. A nucleic acid molecule according to Claim 36 or 37 wherein the molecule comprises the nucleotide sequence of SEQ ID NO:9.
- 20 39. A nucleic acid molecule according to any one of Claims 36 to 38 wherein the molecule comprises the nucleotide sequence of SEQ ID NO:8 and the nucleotide sequence of SEQ ID NO:9.
40. An expression vector comprising a nucleic acid molecule according to any one of Claims 35 to 39.
- 25 41. A host cell comprising a nucleic acid molecule according to any one of Claims 35 to 39 or a vector according to Claim 40.
- 30 42. A method of making a compound according to any one of Claims 1 to 34, or a target specific portion, effector portion or component polypeptide thereof, comprising expressing a nucleic acid molecule according to any one of Claims 35 to 39 in a host cell and isolating the compound, portion or component polypeptide therefrom

43. A pharmaceutical composition comprising a compound according to any one of Claims 1 to 34 and a pharmaceutically acceptable carrier.
- 5 44. A pharmaceutical composition according to Claim 43 wherein the composition is suitable for parenteral administration.
45. A compound according to any one of Claims 1 to 34 for use in medicine.
- 10 46. Use of a compound according to any one of Claims 1 to 34 in the preparation of a medicament for treating a patient with cancer.
- 15 47. A method of treating a patient with cancer, the method comprising administering a compound according to any one of Claims 1 to 34 to said patient.
48. A use according to Claim 46 or a method according to Claim 47 wherein the mammal is a human.
- 20 49. A use according to Claim 46 or a method according to Claim 47 wherein the patient has a solid tumour.
50. A use according to Claim 46 or a method according to Claim 47 wherein the cancer is a glioblastoma.
- 25 51. A compound substantially as described herein with reference to the description and figures.
52. A pharmaceutical composition substantially as described herein with
30 reference to the description and figures.